

Amendments to the Specification

At the indicated page and line number, please insert the following paragraphs:

(Page 1, line 4) This application is a §371 of PCT/US99/06644, filed on March 26, 1999, which claims priority to US Provisional Applications 60/079,759 filed March 27, 1998 and 60/095,153 filed August 3, 1998.

(Page 72, line 1) Please insert a copy of the abstract which attached hereto on a separate sheet.

At the indicated page and line number, please replace the existing paragraphs with the ones set forth below.

(Page 11, line 5) Figure 1 shows the predicted structure of MOAT-B (SEQ ID NO: 2) and comparison with human MRP (SEQ ID NO: 19). The vertical lines indicate identical amino acids and the vertical dots indicate conserved amino acids. Gaps are indicated by periods. The overbars indicate potential transmembrane spanning segments as predicted by the TMAP program. The first and second nucleotide binding folds (NBF 1 and NBF 2) are indicated by horizontal arrows. The C-terminal 34 amino acids (residues 1291-1325) are replaced in the second class of MOAT-B cDNA clones by the following amino acids: ILQKKLSTYWSH (SEQ ID NO: 20). The Alignment was performed using the GAP program (gap weight 3.0, length weight 0.1) in the Genetics Computer Group Package. H. MRP: human MRP.

(Page 11, line 19) Figures 2A and 2B depict a comparison of the nucleotide binding folds and hydropathy profile of MOAT-B with those of other eukaryotic ABC transporters. Fig. 2A shows the comparison of the nucleotide binding folds of MOAT-B (residues 428 to 577 of SEQ ID NO: 2;

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residues 1058 to 1216 of SEQ ID NO: 2). Amino acids that are identical to those of MOAT-B are shaded, and gaps are indicated by periods. Walker A and B motifs, and the ABC transporter family signature sequence C, are underlined. Amino acid positions are indicated to the right. Amino acid sequences were aligned using the PILEUP program (gap weight 3.0, length weight 0.1) in the Genetics Computer Group Package. Fig. #2B shows a comparison of the MOAT-B hydrophathy profile. To facilitate comparison, the proteins are aligned so that the N-terminal nucleotide binding folds (NBF) are roughly in register. NBF's are indicated by bars. Values above and below the horizontal lines indicate hydrophobic and hydrophilic regions, respectively. Hydrophobicity plots were generated using the Kyte-Doolittle algorithm with a window of 7 residues. The transporters shown are: human multidrug-associated protein, H. MRP (P33529; residues 661 to 810 of SEQ ID NO: 19; residues 1310 to 1469 of SEQ ID NO: 19); human multispecific organic anion transporter, H. MOAT (U63970; SEQ ID NO: 23; SEQ ID NO: 24); Saccharomyces cerevisiae yeast cadmium factor 1, S. YCF1 (P39109; SEQ ID NO: 21; SEQ ID NO: 22); rat sulfonylurea receptor, R. SUR (Q09427; SEQ ID NO: 29; SEQ ID NO: 30); human cystic fibrosis transmembrane conductance regulator, H. CFTR (M28668; SEQ ID NO: 25; SEQ ID NO: 26); Leishmania P-glycoprotein, L. PgpA (P21441; SEQ ID NO: 27; SEQ ID NO: 28) and human mdrl gene product, H. MDR1 (P08183; SEQ ID NO: 31; SEQ ID NO: 32). Accession numbers and sequence identifiers for the NBF I and NBF II, respectively, are shown in parentheses.

a 5

(Page 12, line 32) Figures 5A and 5B show the predicted structures of MOAT-C and MOAT-D. Fig. 5A presents the structure of MOAT-C (SEQ ID NO: 4). Fig. 5B shows the structure of MOAT-D (SEQ ID NO: 33). Numbered overbars indicate potential transmembrane spanning helices. Horizontal arrows indicate the positions of the amino terminal (NBF1) and

*(C5
C6)*

C-terminal (NBF2) nucleotide binding folds. Walker A and B motifs, and the ABC transporter family signature sequence C are underlined. Bullets indicate the positions of potential N-linked glycosylation sites that are conserved with previously reported N-glycosylation sites in MRP. The indicated MOAT-C transmembrane spanning helices were predicted using the TMAP program and an input alignment of MOAT-B and MOAT-C. The indicated MOAT-D transmembrane helices are based upon inspection of an alignment with MRP.

(P)

(Page 13, line 15) Figures 6A and 6B show a comparison of the nucleotide binding folds and hydrophathy profiles of MOAT-C (residues 578 to 727 of SEQ ID NO: 4; residues 1210 to 1369 of SEQ ID NO: 4) and MOAT-D (residues 644 to 793 of SEQ ID NO: 6; residues 1306 to 1465 of SEQ ID NO: 6) with those of other related ABC transporters including MOAT-B (residues 428 to 577 of SEQ ID NO: 2; residues 1058 to 1216 of SEQ ID NO: 2). Fig. 6A depicts the comparison of the nucleotide binding folds. The alignment was produced using the PILEUP command (gap weight 3.0, length weight 0.1) in the Genetics Computer Group Package Version 9.1. Amino acid positions conserved in at least 4 of the 8 proteins are shaded. Periods indicate gaps in the alignment. Walker A and B, and the ABC transporter family signature sequence C are indicated by underbars. Fig. 6B shows the comparison of hydrophathy profiles. To facilitate comparisons, gaps were introduced at the N-termini of some proteins in order to bring the first nucleotide binding folds into register. Nucleotide binding folds are indicated by bars. Values above and below the horizontal lines indicate hydrophobic and hydrophilic regions, respectively. Hydrophobicity plots were generated using the Kyte-Doolittle algorithm with a window of 7 residues. Accession numbers are as follows: MRP, P33529 (residues 661 to 810 of SEQ ID NO: 19; residues 1310 to 1469 of SEQ ID NO: 19); cMOAT, U63970 (SEQ ID NO: 23; SEQ ID NO:

(b)(4) Cmt
24) ; SUR, Q09428 (SEQ ID NO: 29; SEQ ID NO: 30) ; CFTR,
P-13569 (SEQ ID NO: 25; SEQ ID NO: 26) ; MDR1, P08183 (SEQ ID
NO: 31; SEQ ID NO: 32) .

(b)(4) A.M.
(Page 14, line 27) Figure 9 shows predicted amino acid sequence of MOAT- E (SEQ ID NO: 8). Also shown are the location of the potential transmembrane helices (overbars), the potential - glycosylation site (black dot) and the two nucleotide binding folds (NBF1 and NBF2). Walker A and B motifs, as well as the signature C motif of ABC transporters, are also indicated.